

REMARKS/ARGUMENTS

The office action of August 22, 2008 has been carefully reviewed and these remarks are responsive thereto. Reconsideration and allowance of the instant application are respectfully requested. Claims 1-8, 11-17, 19-21 remain pending. Claims 12 and 20 have been amended to correct very minor grammatical errors. No new issues or new matter are raised by these amendments.

Claims 1-8, 11-17, 19-21 remain rejected under 35 USC 103(a) over Adams et al. (US 6,403,574) in view of Achard et al. (US 2002/0019383).

The Office Action asserts that the Achard compounds, disclosed as CB1 receptor antagonists are sufficiently "close" in structure to those of the Adams GABA_A inhibitors for the skilled man to assume the Adams compounds would be CB1 antagonists. This position is respectfully traversed.

As noted in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007) "While the KSR Court rejected a rigid application of the teaching, suggestion or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying 'a reason' that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination. (emphasis added)" Further in *Innogenetics, N.V., v. Abbott Laboratories*, 512 F.3d 1363 (Fed. Cir. 2008) "We must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention."

"Sufficiently close" is not "a reason" that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." Moreover, as discussed below, the compounds of Adams and Achard are not so "sufficiently close" that one skilled in the art would have modified Adams in view of Achard to arrive at the instant claims.

There are significant structural differences between the Achard and Adams compounds and the Office Action fails to address these structural differences. Instead the differences are sidestepped by paraphrasing the structure of the Adams compounds at a high

enough level of generality to superficially support the "very close" position.

The Office Action now considers that the Achard compounds are:

".. . similar insofar as they have the same core structure where substituents attach from the position 1 nitrogen and position 3 carbon"

This general statement is accurate, but the specific substituents attached to each of Adams and Achard are completely different. Adams' nitrogen has an amide attached to the core nitrogen whereas Achard has a disubstituted methyl substituent R_2R_3CH- , and the Adams core carbon has an ether substituent whereas Achard has the amide or reverse amide substituent R1. These are significant differences that are simply not addressed.

It is well known that modulation of receptors, such as the CB1 receptor, depends on a very close interaction of the tertiary structure and charge properties of the modulator compound with the complex tertiary and charge structure of the receptor sequence. It is too simplistic to say that because both Achard and Adams have an azetidine core with substituents on the nitrogen and 3-carbon, they are expected to have the same CB1 antagonistic activity irrespective of the rather major differences in what those substituents actually are.

The Office Action's second comment that "They may also contain similar substituents such as a carbamine and a phenyl group" does not address the fact that the substituents on the core azetidine ring are completely different. The modification of Adams in view of Achard can only be made through hindsight afforded by the claimed invention.

As previously noted, Adams does not teach the use of its disclosed compounds for treatment of a disorder selected from the group consisting of obesity, excessive food intake, and smoking as claimed in amended claim 1. Moreover, the use of the disclosed compounds as claimed are not obvious applications of the Adams compounds. The molecular target disclosed in Adams is the GABA_A receptor, and modulation of the GABA_A receptor is not known in the art to be involved with the claimed disorders. Thus Adams does not suggest that GABA_A receptor modulators would be useful for the now-claimed disorders. Achard does not remedy the defects of Adams.

As discussed above, the Achard compounds are not "very close" in structural similarity to those of Adams and the present application. Achard (a) does not have an amide moiety attached to the azetidine nitrogen, and (b) does not have the ether link to the ring carbon in position 3 of the azetidine ring. The only similarity between the Achard and

Adams compounds seems to be the common possession of an azetidine ring.

One skilled in the art would not have had any reasonable expectation that the instant compounds were suitable for the treatments as claimed in view of Archard. Withdrawal of this rejection is requested.

CONCLUSION

If any further fees are required or if an overpayment is made, the Commissioner is authorized to debit or credit our Deposit Account No. 19-0733, accordingly.

All rejections having been addressed, applicants respectfully submit that the instant application is in condition for allowance, and respectfully solicit prompt notification of the same.

Respectfully submitted,

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